Investigating the functionality of an OCT4-short response element in human induced pluripotent stem cells.

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Public Summary:
Pluripotent stem cells offer great therapeutic promise for personalized treatment platforms for numerous injuries, disorders, and diseases. Octamer-binding transcription factor 4 (OCT4) is a key regulatory gene maintaining pluripotency and self-renewal. With gene correction in regenerative medicine and cell transplantation, use of the this regulatory element may have advantages when expressing a suicide gene if stem cells remain in the final product of cells to be transplanted. However, this gene regulatory element region is very large in size, thus limiting how it can be used to help protect the safety or a regenerative medicine cell product. The purpose of this investigation was to characterize a shortened version of OCT4 element during stem cell manipulation and to examine its response during differentiation to mature cells. Our findings demonstrate that the OCT4-short response element is active in during early stem cell manipulation and is inactivated when pluripotent cells differentiate. These studies demonstrate that this shortened OCT4 regulatory element is functional and may be useful as part of a safety component in a gene transferring system that could be used as an efficient and clinically applicable safety platform for gene transfer in regenerative medicine.

Scientific Abstract:
Pluripotent stem cells offer great therapeutic promise for personalized treatment platforms for numerous injuries, disorders, and diseases. Octamer-binding transcription factor 4 (OCT4) is a key regulatory gene maintaining pluripotency and self-renewal of mammalian cells. With site-specific integration for gene correction in cellular therapeutics, use of the OCT4 promoter may have advantages when expressing a suicide gene if pluripotency remains. However, the human OCT4 promoter region is 4 kb in size, limiting the capacity of therapeutic genes and other regulatory components for viral vectors, and decreasing the efficiency of homologous recombination. The purpose of this investigation was to characterize the functionality of a novel 967bp OCT4-short response element during pluripotency and to examine the OCT4 titer-dependent response during differentiation to human derivatives not expressing OCT4. Our findings demonstrate that the OCT4-short response element is active in pluripotency and this activity is in high correlation with transgene expression in vitro, and the OCT4-short response element is inactivated when pluripotent cells differentiate. These studies demonstrate that this shortened OCT4 regulatory element is functional and may be useful as part of an optimized safety component in a site-specific gene transferring system that could be used as an efficient and clinically applicable safety platform for gene transfer in cellular therapeutics.